



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Peter S. Linsley et al.  
Serial N .: 09/609,915  
Filed: July 3, 2000  
Docket: 30436.30USI2  
Title: SOLUBLE CTLA4 MUTANT MOLECULES AND USES THEREOF

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CERTIFICATE UNDER 37 CFR 1.8

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By:   
Name: Tracy Truick

Assistant Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Madam/Sir:

We are transmitting herewith the attached:

- ☒ Transmittal sheet, in duplicate, containing Certificate under 37 CFR 1.8.
- ☒ Supplemental Information Disclosure Statement (37 C.F.R. §1.97 (b)(3))
- ☒ Form 1449 (Information Disclosure Statement)
- ☒ Exhibits 221-258
- ☒ Return postcard

Please charge any additional fees or credit overpayment to Deposit Account No. 50-0306. A duplicate of this sheet is enclosed.

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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

**Applicant:** Peter S. Linsley et al. **Examiner:** M. Lazar Wesley, Ph.D.  
**Serial No.:** 09/609,915 **Group Art Unit:** 1646  
**Filed:** July 3, 2000 **Docket No.:** 30436.30USI2  
**Title:** SOLUBLE CTLA4 MUTANT MOLECULES AND USES THEREOF

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**CERTIFICATE UNDER 37 CFR §1.8:**

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By:   
Name: Tracy Traick

55 South Lake Avenue, Suite 710  
Pasadena, California 91101  
June 17, 2003

**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT**  
**(37 C.F.R. § 1.97(b)(3))**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

This information Disclosure Statement should be considered because it is submitted before the mailing date of the first Office Action on the merits according to 37 C.F.R. §1.97(b)(3). In accordance with 37 C.F.R. §1.98(d), copies of Exhibits 221-258 as set forth in the Form 1449 are included herewith.

With regard to the above-identified application, the items of information listed on the enclosed Form 1449 are brought to the attention of the Examiner. They are as follows:

- International Publication No. WO 98/31820 published July 23, 1998. **(Exhibit 221)**
- International Publication No. WO 94/28912 published December 22, 1994.  
**(Exhibit 222)**

- U.S. Patent No. 6,444,792 issued September 3, 2002. **(Exhibit 223)**
- International Publication No. WO 93/19767 published October 14, 1993. **(Exhibit 224)**
- International Publication No. WO 94/29436 published December 22, 1994.  
**(Exhibit 225)**
- International Publication No. WO 95/33823 published December 14, 1995.  
**(Exhibit 226)**
- U.S. Patent No. 5,770,197 issued June 23, 1998. **(Exhibit 227)**
- U.S. Patent No. 6,132,992 issued October 17, 2000. **(Exhibit 228)**
- U.S. Patent No. 6,090,914 issued July 18, 2000. **(Exhibit 229)**
- U.S. Patent No. 5,773,253 issued June 30, 1998. **(Exhibit 230)**
- U.S. Patent No. 5,977,318 issued November 2, 1999. **(Exhibit 231)**
- U.S. Patent No. 5,885,579 issued March 23, 1999. **(Exhibit 232)**
- U.S. Patent No. 5,993,800 issued November 30, 1999. **(Exhibit 233)**
- U.S. Patent No. 5,916,560 issued June 29, 1999. **(Exhibit 234)**
- European Patent Publication Number 0 613 944 A2 published September 7, 1994.  
**(Exhibit 235)**
- Peach et al., "Complementarity Determining Region 1 (CDR1)- and CDR3-analogous in CTLA-4 and CD28 Determine the Binding to B7-1," (1994) J. Exp. Med. 180:2049-2058. **(Exhibit 236)**
- Morton et al., "Differential Effects of CTLA-4 Substitutions on the Binding of Human CD80 (B7-1) and CD86 (B7-2)," (1996) J. Immunol. Feb 1; 156:1047-1054.  
**(Exhibit 237)**
- International Publication No. WO 98/56417 published December 17, 1998 –  
**(Exhibit 238)**
- Sun, Hong et al., "Prevention of Chronic Rejection in Mouse Aortic Allografts by Combined Treatment with CTLA4-Ig and Anti-CD40 Ligand Monoclonal Antibody," *Transplantation*, 1997, 64:1838-56 **(Exhibit 239)**

- Souza, "Synergistic inhibition of established collagen induced arthritis (CIA) through dual inhibition of ICAM-1 and CD40L pathways," *Arthritis and Rheumatism*, 1999, page S60; abstract 64 (**Exhibit 240**)
- Blazar, Bruce R. et al., "Coblockade of the LFA1:ICAM and CD28/CTLA4:B7 Pathways Is A Highly Effective Means of Preventing Acute Lethal Graft-Versus-Host Disease Induced by Fully Major Histocompatibility Complex-Disparate Donor Grafts," *Blood*, 1995, 85:2607-18 (**Exhibit 241**)
- U.S. Patent No. 5,968,510 issued October 19, 1999 (**Exhibit 242**)
- International Publication No. WO 01/92337 published December 6, 2001 (**Exhibit 243**)
- Alegre et al., "Immunomodulation of transplant rejection using monoclonal antibodies and soluble receptors," *Dig. Dis. Sci.*, 1995, 40:58-64 (**Exhibit 244**)
- Murakami et al., "Identification and characterization of an alternative cytotoxic T lymphocyte-associated protein 4 binding molecule on B cells," *Proc. Nat. Acad. Sci. USA*, 1996, 93:7838-7842 (**Exhibit 245**)
- Peach et al., "Both extracellular immunoglobulin-like domains of CD80 contain residues critical for binding T cell surface receptors CTLA-4 and CD28," *J. Biol. Chem.*, 1995, 270:21181-21187 (**Exhibit 246**)
- Fargeas et al., "Identification of Residues in the V Domain of CD80 (B7-1) Implicated in Functional Interactions with CD28 and CTLA4," *J. Exp. Med.*, 1995, 182:667-675 (**Exhibit 247**)
- Steurer et al., "Ex Vivo Coating of Islet Cell Allografts with Murin CTLA4/Fc Promotes Graft Tolerance," *J. Immunol.*, 1995, 155:1165-1174 (**Exhibit 248**)
- Guo et al., "Mutational Analysis and an Alternatively Spliced Product of B7 Defines Its CD28/CTLA4-binding Site on Immunoglobulin C-like Domain," *J. Exp. Med.*, 1995, 181:1345-1355 (**Exhibit 249**)

- Peach et al., "CTLA4Ig: A Novel Immunoglobulin Chimera with Immunosuppressive Properties," *Methods*, 1995, 8:116-123 (**Exhibit 250**)
- Rattis et al., "Expression and function of B7-1 (CD80) and B7-2 (CD86) on human epidermal Langerhans cells," *Eur. J. Immunol.*, 1996, 26:449-453 (**Exhibit 251**)
- International Publication No. WO 98/33513 published August 6, 1998 (**Exhibit 252**)
- International Publication No. WO 02/02638 published January 10, 2002 (**Exhibit 253**)
- U.S. Patent No. 5,958,403 issued September 28, 1999. (**Exhibit 254**)
- Najafian, et al., "CTLA4-Ig: a novel immunosuppressive agent," *Exp. Opin. Invest. Drugs*, 2000, 9:2147-2157 (**Exhibit 255**)
- European Patent Publication Number 0 682 039 A1 published November 15, 1995. (**Exhibit 256**)
- Schwartz, R., "Costimulation of T Lymphocytes: The Role of CD28, CTLA-4, and B7/BB1 in Interleukin-2 Production and Immunotherapy," *Cell*, 1992, 71:1085-1088. (**Exhibit 257**)
- U.S. Patent No. 5,637,481 issued June 10, 1997 (**Exhibit 258**)

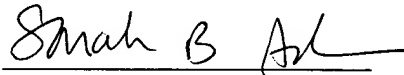
No representation is made that a reference is "prior art" within the meaning of 35 U.S.C. §§ 102 and 103 and Applicants reserve the right, pursuant to 37 C.F.R. § 1.131 or otherwise, to establish that the references are not "prior art." Moreover, Applicants do not represent that the references have been thoroughly reviewed or that any relevance of any portion of a reference is intended.

Consideration of the items listed is respectfully requested. Applicants invite the Patent Office to request additional information if necessary. Pursuant to the provisions of M.P.E.P. 609, it is requested that the Examiner return a copy of the attached Form 1449, marked as being considered and initialed by the Examiner, to the undersigned with the next official communication.

Peter S. Linsley et al.  
U.S. Serial No. 09/609,915  
Filed: July 3, 2000  
Page 5

No fee is deemed necessary in connection with the filing of this Information Disclosure Statement. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee, or credit any overpayment, to Deposit Account No. 50-0306.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Sarah B. Adriano", written over a horizontal line.

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FORM 1449\*

**INFORMATION DISCLOSURE STATEMENT  
IN AN APPLICATION**

(Use several sheets if necessary)

Docket Number

30436.30USI2

Application Number

09/609,915

Applicant

Peter S. Linsley et al.

Filing Date

July 3, 2000

Group Art Unit

1646

**U.S. PATENT DOCUMENTS**

EXAMINER INITIAL	DOCUMENT NO.	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	6,444,792 (Exhibit 223)	September 3, 2002	Gray et al.			January 8, 1999
	5,770,197 (Exhibit 227)	June 23, 1998	Peter S. Linsley et al.			January 22, 1993
	6,132,992 (Exhibit 228)	October 17, 2000	Jeffrey A. Ledbetter et al.			October 5, 1995
	6,090,914 (Exhibit 229)	July 18, 2000	Peter S. Linsley et al.			April 15, 1994
	5,773,253 (Exhibit 230)	June 30, 1998	Peter S. Linsley et al.			July 21, 1995
	5,977,318 (Exhibit 231)	November 2, 1999	Peter S. Linsley et al.			June 7, 1995
	5,885,579 (Exhibit 232)	March 23, 1999	Peter S. Linsley et al.			July 8, 1997
	5,993,800 (Exhibit 233)	November 30, 1999	Peter S. Linsley et al.			June 6, 1995
	5,916,560 (Exhibit 234)	June 29, 1999	Christian P. Larsen et al.			March 20, 1997
	5,968,510 (Exhibit 242)	October 19, 1999	Linsley et al.			October 4, 1996
	5,958,403 (Exhibit 254)	September 28, 1999	Strom et al.			July 11, 1994
	5,637,481 (Exhibit 258)	June 10, 1997	Ledbetter et al.			September 13, 1993

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.

\*Substitute Disclosure Statement Form (PTO-1449) Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

FORM 1449\*

Docket Number

30436.30USI2

Application Number

09/609825

**INFORMATION DISCLOSURE STATEMENT  
IN AN APPLICATION**

(Use several sheets if necessary)

Applicant

Peter S. Linsley et al.

Filing Date

July 3, 2000

Group Art Unit

1646

**FOREIGN PATENT DOCUMENTS**

	DOCUMENT NO.	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
						YES	NO
	WO 98/31820 (Exhibit 221)	July 23, 1998	PCT				
	WO 94/28912 (Exhibit 222)	December 22, 1994	PCT				
	WO 93/19767 (Exhibit 224)	October 14, 1993	PCT				
	WO 94/29436 (Exhibit 225)	December 22, 1994	PCT				
	WO 95/33823 (Exhibit 226)	December 14, 1995	PCT				
	EP 0 613 944 A2 (Exhibit 235)	September 7, 1994	EPO				
	WO 98/56417 (Exhibit 238)	December 17, 1998	PCT				
	WO 01/92337 (Exhibit 243)	December 6, 2001	PCT				
	WO 98/33513 (Exhibit 252)	August 6, 1998	PCT				
	WO 02/02638 (Exhibit 253)	January 10, 2002	PCT				
	EP 0 682 039 A1 (Exhibit 256)	November 15, 1995	EPO				

**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)**

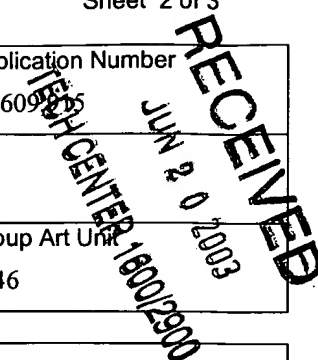
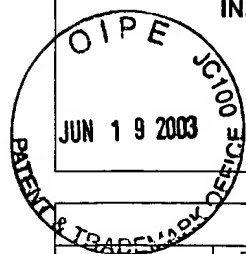
		Peach et al., "Complementarity Determining Region 1 (CDR1)- and CDR3-analogous in CTLA-4 and CD28 Determine the Binding to B7-1," (1994) J. Exp. Med. 180:2049-2058. (Exhibit 236)
		Morton et al., "Differential Effects of CTLA-4 Substitutions on the Binding of Human CD80 (B7-1) and CD86 (B7-2)," (1996) J. Immunol. 156:1047-1054. (Exhibit 237)
		Sun, Hong et al., "Prevention of Chronic Rejection in Mouse Aortic Allografts by Combined Treatment with CTLA4-Ig and Anti-CD40 Ligand Monoclonal Antibody," Transplantation, 1997, 64:1838-56 (Exhibit 239)

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Application Number

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## Applicant

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## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

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